CLAIMS

We claim:

1. A method of treatment or prevention of at least one degenerative disorder of muscle, bone, or glucose homeostasis comprising administering an effective amount of a pharmaceutical composition to a mammal, wherein the composition comprises an ActRIIB fusion polypeptide comprising (a) a first amino acid sequence derived from the ActRIIB extracellular domain and (b) a second amino acid sequence derived from the Fc portion of an antibody; and allowing the composition to inhibit GDF-8 activity.
2. The method of claim 1, wherein the mammal is human.
3. The method of claim 1, wherein the pharmaceutical composition is administered to a mammal in need of treatment or prevention of a disorder chosen from at least one of muscle disorder, neuromuscular disorder, and bone degenerative disorder.
4. The method of claim 1, wherein the pharmaceutical composition is administered to a mammal in need of treatment or prevention of a disorder chosen from at least one of muscular dystrophy, Duchenne's muscular dystrophy, muscle atrophy, organ atrophy, carpal tunnel syndrome congestive obstructive pulmonary disease, sarcopenia, cachexia, muscle wasting syndrome, and amyotrophic lateral sclerosis.

5. The method of claim 1, wherein the pharmaceutical composition is administered to a mammal in need of treatment or prevention of Duchenne's muscular dystrophy.

6. The method of claim 1, wherein the pharmaceutical composition is administered to a mammal in need of treatment or prevention of a disorder chosen from at least one of obesity and adipose tissue disorder.

7. The method of claim 1, wherein the pharmaceutical composition is administered to a mammal in need of treatment or prevention of a disorder chosen from at least one of syndrome X, impaired glucose tolerance, trauma-induced insulin resistance, and type 2 diabetes.

8. The method of claim 1, wherein the pharmaceutical composition is administered to a mammal in need of treatment or prevention of at least one of type 2 dibetes and obesity.

9. The method of claim 1, wherein the pharmaceutical composition is administered to a mammal in need of treatment or prevention of a disorder chosen from at least one of osteoarthritis and osteoporosis.

10. The method of claim 1, wherein the pharmaceutical composition is administered to a mammal in need for repair of damaged muscle.

11. The method of claim 9, wherein the damaged muscle is myocardiac muscle or diaphragm.

12. The method of claim 1, wherein said ActRIIB fusion polypeptide is administered at the effective amount chosen from 1 μ/kg to 20 mg/kg, 1

μg/kg to 10 mg/kg, 1 μg/kg to 1 mg/kg, 10 μg/kg to 1 mg/kg, 10 μg/kg to 100 μg/kg, 100 μg to 1 mg/kg, and 500 μg/kg to 1 mg/kg.

13. The method of claim 1, wherein the first amino acid sequence of said ActRIIB fusion polypeptide comprises amino acids 23 to 138 of SEQ ID NO:3.

14. The method of claim 1, wherein the first amino acid sequence of said ActRIIB fusion polypeptide comprises amino acids 19 to 144 of SEQ ID NO:1.

15. The method of claim 1, wherein the second amino acid sequence of said ActRIIB fusion polypeptide comprises a sequence chosen from (a) the Fc fragment of IgG, (b) the Fc fragment of IgG_1, (c) the Fc fragment of IgG_4, and (d) amino acids 148 to 378 of SEQ ID NO:3.

16. The method of claim 1, wherein the sequence of the ActRIIB fusion polypeptide is set out in SEQ ID NO:3.

17. The method of claim 1, wherein circulatory half-life of the ActRIIB fusion polypeptide exceeds 5 days.

18. A fusion protein comprising the amino acid sequence of SEQ ID NO:3.

19. An isolated nucleic acid encoding the fusion protein of claim 18.

20. The nucleic acid of claim 19, whein said nucleic acid is set out in SEQ ID NO:4.

21. An expression vector, comprising the nucleic acid of claim 19.

22. A host cell comprising the vector of claim 21.

23. The method of claim 1, wherein the fusion protein is encoded by a nucleic acid that hybridizes to the sequence of SEQ ID NO:4 under stringent hybridization conditions.

24. A method for identifying inhibitors of GDF-8, comprising:

(a) preparing a first binding mixture comprising the ActRIIB fusion polypeptide of claim 18 and GDF-8;

(b) measuring the amount of binding between the ActRIIB fusion polypeptide and GDF-8 in the first mixture;

(c) preparing a second binding mixture comprising the ActRIIB fusion polypeptide, GDF-8, a test compound; and

(d) measuring the amount of binding between the ActRIIB fusion polypeptide and GDF-8 in the second mixture.

25. A method of inhibiting GDF-8 activity, comprising contacting GDF-8 with a composition, wherein the composition comprises an ActRIIB fusion polypeptide comprising (a) a first amino acid sequence derived from the ActRIIB extracellular domain and (b) a second amino acid sequence derived from the Fc portion of an antibody; and allowing the composition to inhibit GDF-8 activity.

26. A method of increasing muscle strength, said method comprising administering a therapeutically effective amount of the ActRIIB fusion polypeptide to a mammal, thereby increasing muscle strength, wherein the ActRIIB fusion polypeptide comprising (a) a first amino acid sequence derived from the ActRIIB extracellular domain and (b) a

second amino acid sequence derived from the Fc portion of an antibody.

27. A method of increasing trabecular bone density, said method comprising a administering a therapeutically effective amount of the ActRIIB fusion polypeptide to a mammal, thereby increasing trabecular bone density, wherein the ActRIIB fusion polypeptide comprising (a) a first amino acid sequence derived from the ActRIIB extracellular domain and (b) a second amino acid sequence derived from the Fc portion of an antibody.

28. A method of increasing glucose tolerance, said method comprising a administering a therapeutically effective amount of the ActRIIB fusion polypeptide of to a mammal, thereby increasing trabecular bone density, wherein the ActRIIB fusion polypeptide comprising (a) a first amino acid sequence derived from the ActRIIB extracellular domain and (b) a second amino acid sequence derived from the Fc portion of an antibody.